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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,394	12/12/2005	Carl Gustav Figdor	ALXN-PO1-095	6059

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EXAMINER
LI, RUIXIANG

ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,394	FIGDOR ET AL.	
	Examiner	Art Unit	
	RUIXIANG LI	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19 and 22-41* is/are rejected.

7)☒ Claim(s) *20 and 21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicants' amendment filed on 12/08/2008 has been entered. Claims 1-18 are canceled. Claims 19-25 are amended. Claims 33-41 are added. Claims 19-41 are pending and under consideration.

Withdrawn Objections and/or Rejections

The objection to claim 22 is withdrawn in view of amended claim.

The objection to the title of the invention is withdrawn in view of amended title.

The rejection of claims 19-25 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is replaced with a scope of enablement rejection under 35 U.S.C. 112, first paragraph in view of amended claim 19 and new claims 33-41.

Claim Rejections under 35 USC § 112, 1st paragraph

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii). Claims 33-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was

not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 33 recites “contacting a sample of cells with: (i) an agent that binds to DC-SIGN and (ii) an antibody that binds to CD68, or antigen-binding fragment thereof, wherein said sample of cells is a synovial tissue sample obtained from a person with rheumatoid arthritis; and isolating cells that bind to (i) and (ii), to thereby isolate macrophages that express DC-SIGN", which introduce new matter. There is no support for such a method in the instant disclosure.

(iii). Claims 19 and 22-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for enriching the percentage of macrophages in a sample of cells using an antibody that binds to DC-SIGN, does not reasonably provide enablement for a method for enriching the percentage of macrophages in a sample of cells using an agent that binds to DC-SIGN and a method for isolating macrophages that express DC-SIGN comprising contacting a sample of cells with (i) an agent that binds to DC-SIGN and (ii) an antibody that binds to CD68. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The previous office action states that an agent that binds DC-SIGN will bind to both macrophages and dendritic cells. Such an agent cannot be used in the claimed method to separate macrophages from dendritic cells (page 4, the 4th paragraph). The amendment has resolved this issue. However, the enablement issue with respect to the agents that bind DC-SIGN remains (see page 4, the 3rd paragraph and page 5, the 2nd paragraph of the previous office action).

Beginning at page 8 of Applicants' response, Applicants, citing MPEP and case law, argue that it is not required for enablement of the claims that the specification or the art exemplify the use of each possible species of a claimed genus. Applicants argue that the specification discloses a variety of genera and subgenera of suitable agents that binds to DC-SIGN, including, without limitation, anti-SIGN antibodies or antigen-binding fragments thereof, sugars, antibiotics, and proteins. Applicants argue that of each genus of agents were also known in the art at the priority date of the application and described in the specification.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. While providing sufficient guidance and working examples on how to isolate DC-SIGN-expressing cells using an antibody that binds DC-SIGN (see e.g., paragraphs [0064], [0065], [0089]), the specification fails to provide sufficient guidance and/or working examples with respect to how to use an agent other than an antibody to isolate DC-SIGN-expressing cells. The specification states that an agent

that binds DC-SIGN can be, for example, affixed to a solid support and a sample of cells can be contacted to said support and the support can then be washed to remove cells not bound by the agent. The specification also asserts that such agents can include various carbohydrates, lectins, antibiotics, sugars, and antibodies (paragraph [0089]). However, such a disclosure fails to provide sufficient directions on how to use such a broad genus of agents to purify macrophages in the synovium of rheumatoid arthritis patients.

While the specification and the prior art teach that DC-SIGN binds gp120 and ICAM-3/ICAM-2, there is no specific guidance provided in the specification on how to use these proteins to isolate DC-SIGN-expressing cells. Moreover, there is no conserved structural limitation for the proteins to be used for binding to DC-SIGN. In fact, DC-SIGN does not bind ICAM-1 (J. Leukocyte Biology, 71:921-931, June 2002; in particular page 922, right column, line 18). Thus, such a disclosure does not enable the subgenus of proteins recited in the claims. Likewise, while the specification asserts that various carbohydrates and sugars can be used to purify macrophages in the synovium of rheumatoid arthritis patients (paragraph [0089]), there are no specific directions provided how to use the broad subgenus of carbohydrates and sugars, which cover carbohydrates from polysaccharides (e.g., glycogen, starch, dextran), oligosaccharides, to monosaccharides. The prior art teaches that DC-SIGN recognizes high-mannose residues located more internally within a glycan structure, but not single terminal mannose residues (J. Leukocyte Biology, 71:921-931, June 2002; in particular page

922, left column, lines14-15; right column, lines 22-25). Also, the prior art teaches sugars such as N-acetyl-D-glucosamine and galactose bind less potent to DC-SIGN (column 6, lines 8-9). Thus, it is unpredictable whether a given protein, a carbohydrate, lectin, or an antibiotic binds DC-SIGN in such a way that it can be used to purify macrophages in the synovium of rheumatoid arthritis patients. It would require undue experimentation for one of skilled in the art to practice the claimed method commensurate in scope with these claims.

Applicants argue that the common structural characteristics of ligands that bind to DC-SIGN were known in the art at the time of filing. Applicants argue that Geijtenbeek et al. teach that the "EPN or QPD" sequences within the CRD of DC-SIGN are essentially in recognizing mannose- ad galactose-containing structures, respectively. Applicants argue that Geijtenbeek et al. teach that DC-SIGN recognizes high-mannose residues located more internally within a glycan structure. Applicants argue that one of skill in the art reading the specification would be able to determine whether a sugar or an antibiotic can bind to DC-SIGN based on its structure, in light of the general knowledge in the art.

Applicants' argument has been fully considered, but is not deemed to be persuasive because the "EPN or QPD" sequences within the CRD of DC-SIGN do not provide teachings on the conserved structure of the genus of agents that bind DC-SIGN. In contrast, the teachings of Geijtenbeek et al. evidences that the genus of sugar is not enabled. There is no specific guidance and/or working example on how to use a

sugar/carbohydrate to isolate macrophages. Furthermore, Geijtenbeek et al. do not provide teachings with respect to how to use these sugars and antibiotics to isolate macrophages in the synovium of rheumatoid arthritis patients.

Applicants argue that methods for determining whether an agent binds to DC-SIGN were well known in the art of molecular biology at the priority date of the application and are described in the specification. This is not found to be persuasive because one of skilled in the art would have to screen an agent that binds DC-SIGN before the claimed method can be practiced. Since the claims do not recite any particular conserved structure for the agents that bind DC-SIGN, it would take undue experimentation for one of skill in the art to screen the candidate agents that are can be used in the claimed methods.

Claim Rejections under 35 USC § 112, 2nd paragraph

(i). The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(ii). Claims 26 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 26 and 39 are indefinite because they recite the limitation “wherein said synovial tissue sample is a synovial fluid sample”. A synovial tissue sample cannot be a synovial fluid sample.

Claim Objections

Claims 20 and 21 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).
A shortened

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/
Primary Examiner, Art Unit 1646

March 5, 2009